REMARKS / ARGUMENTS

In response to the final Office Action of March 26, 2010, Applicants have amended claim 1, and cancelled claim 2, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of presently examined claims 1-3 is respectfully requested.

In the March 26, 2010 office action, claims 1 and 2 have been objected to because they both use different abbreviations to denote kilo Daltons. By this amendment, claim 2 has been canceled. The subject matter of claim 2 is now recited in claim 1 and claim 1 is consistent in reciting "kDa" as the abbreviation for kilo Daltons. Withdrawal of the objection to claim 1 is therefore respectfully requested.

Rejection of claims 2 and 3 over Ma et al.

In the March 26, 2010 final office action, claims 2 and 3 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Ma et al. (U.S. Patent No. 5,786,221). Ma et al. has been cited for allegedly disclosing a pancreatic antigen which is 34 kD according to SDS-PAGE. The Examiner has specifically cited column 6, lines 32-44 for this teaching.

Applicants respectfully submit that the teaching provided by Ma et al. at column 6, lines 34-44 is in relation to an *extract of pancreas tissue*. Studying the lines appearing immediately before and after the cited lines, i.e., lines 25-46, it becomes apparent that the extract containing various protein bands, including one of 34 KD is derived from macerated pancreas:

> In selecting a mammal preferably rodent, most preferably rat strain for use in accordance with the invention, one needs to screen a typical pancreas from the strain or species. The *pancreas* of each suspected strain and/or species is carefully dissected, out, washed in cold PBS and cut into small pieces. An ***extract*** is prepared by suspending one gland in 2-5 ml of cold PBS, homogenized briefly in ice bath and sonicated briefly in ice bath. A detergent (octyl-B-D-glucopyranoside) is then added. After removing debris by centrifugation, protein concentration of extract is determined . . . Extracts that produce one or more band with clinically confirmed IDDM positive sera pool but not with the IDDM negative sera pool will be selected. Desirably, the extract should produce two or more confirmatory bands, preferably at least a 59 KD and 67 KD bands and most preferably a pancreas that includes 90 KD, 59 KD, 67 KD and 34 KD proteins. Such pancreas can then be used a s source of pancreatic antigens for binding to a water insoluble carrier-lectin conjugate. (emphasis added).

See also Example 1 of Ma et al. By this amendment, claim 2 has been canceled and the subject matter previously recited therein has been incorporated into claim 1. The relevant portion of presently amended claim1 reads: "said carcinoma-specific antigen characterized by a molecular weight of about 36 to about 38 kD as determined by SDS-PAGE when isolated from sera or other bodily fluids of pancreatic cancer patients". Since Ma et al. do not teach an antigen which when isolated from pancreas is about 43.5 kDa and when isolated from sera and other bodily fluids of pancreatic cancer patients is about 36 to about 38 KD, the presently claimed invention is distinguished from Ma et al.

Moreover, the auto antibodies on which Ma et al. are based are all directed against the insulin producing beta cells of the pancreatic islets i.e. the endocrine organ of the pancreas and not against the cells or cell surface Ag of the exocrine acinar, duct and centroacinar cells of the exocrine pancreas as are Applicants.

Since the Solid Phase Assay of Ma et al. allegedly identifies selective auto antibodies against the beta-cells of the endocrine pancreatic islets, the antigens and specifically those with MW of 90 kD, 67kD and 34kD are identified as islet-specific antigens. The antigens are expressed also on normal islet cells which react also with auto antibodies present in the sera of their patients with IDDM. In addition, the antigens cited in Ma et al. all bind to lectin.

In contrast, Applicants 3C4-Ag is not found in normal or malignant pancreatic islet cells. The 3C4-Ag is identified by mAb 3C4 has a MW in reduced and nonreduced form of 42-43.5kD and is expressed only on the surface membrane of malignantly transformed (i.e. cancer) cells of the **exocrine** pancreas. The 3C4-Ag does not bind to lectins since it is not at all or only minimally glycosylated. Upon extensive deglycosylation the 3C4-Ag did not change its MW nor did it loose its reactivity with mAb 3C4. *See* specification, page 61. Based on the foregoing remarks and amendments, withdrawal of the rejection of claims 2 and 3 as applied to presently amended claim 1 and previously presented claim 3 is therefore warranted.

Rejection of Claims 1-3 over Hobbs et al. as evidenced by Escribano-Crepso et al.

The rejection of claims 1-3 under 35 U.S.C. 102(b) as allegedly anticipated by Hobbs et al. (*Oncodevelopmental Biology and Medicine1*:37-48, 1980) as evidenced by Escribano-Crespo et al., US Patent No. 4,843,019, issued June 27, 1989, has been maintained.

Hobbs et al. is relied upon for allegedly teaching a pancreatic antigen which is 40 kDa and found in foetal pancreas and carcinoma of the pancreas and not in normal pancreas. Column 1, lines 16-33 of Escribano-Crespo et al. is cited as evidentiary of Figure 2, caption on page 39 of Hobbs et al.

Applicants respectfully submit that while it is true that Hobbs et al. disclose a pancreatic oncofetal antigen (POA) having a molecular weight of 40,000 Daltons, as described on page 44 of the reference, the result of immunohistochemical studies show the antigen is localized in the **cytoplasm** of the secretory cells of adenocarcinoma and that staining also occurs nearby in the stroma and in the lumen of the ducts. *See* page 42, last sentence before Table II, to page 44, first three lines. The authors conclude that POA is secreted by carcinoma cells which may explain its relatively high levels in the serum. Again on page 47 of the reference, Hobbs et al. state "thus far, the only staining that has been seen has been cytoplasmic, predominantly in cells which look as if they have secretory function and there has been some staining in nearby stroma or ducts further suggesting that POA is actually secreted."

In contrast, the presently claimed invention is directed to a single antigen, which presents itself in two different sizes, depending on where it is found. Applicants' presently claimed 43.5 kDa antigen is primarily localized on the *surface* of rat and human pancreatic exocrine cancer cells. *See* specification, Example 12. It is not found on (nor in) pancreatic islet cells nor on (or in) gastric or colon cancer cells as is POA. *See* Applicants' specification, pages 61 and 62, Table 3, compared to Hobbs et al., page 42.

In view of the foregoing remarks, it is evident that the presently amended claims are distinguished from Hobbs et al. and withdrawal of the rejection of claims 1-3 over Hobbs et al. as evidenced by Escribano-Crepso et al. is therefore warranted.

Rejection of claims 1 and 3 over Glassy et al.

Claims 1 and 3 remain rejected under 35 U.S.C. 102(e) as allegedly anticipated by Glassy et al. (U.S. Patent Publication Number 2002/0098581, filed December 20, 2001. Glassy et al. is cited for allegedly teaching an antigen known as SK1 having a molecular weight of 42-46 kDa according to SDS-PAGE.

As presently amended, claims 1 and 3 are distinguished from Glassy et al. for the following reasons.

As disclosed in Example 1 of Glassy et al., the SKI Ag of Glassy et al. was originally identified in Duke's "B' HuColon Carcinoma cells by a human mAb made against these cells. Consequently, the SKI Ag has been found to be present in high frequency in Hu Colon Ca and in several other human cancer cells (colon, gastric, pancreas, lung) and to a lesser extent i.e. in lesser numbers on the surface membrane of normal cells. The HumAbs raised against the SKI Ag were made purposely to react with any cancer cell that expresses the SKI. Enzyme treatment, SDS -PAGE and immunoblotting of the SKI Ag showed that (1) SKI is sensitive to neuraminidase in addition to trypsin, periodate and heat, abolishing the reactivity with humAb against SKI, i.e. the SKI Ag was a sialoglycoprotein; (2) SKI is found to be a doublet of 42-46 kD. SKi antigen is also present intracellularly and even in the nucleus (*see* page 11) of Hu Colon Ca cells. The SKI antigen appears to retain the MW of the doublet upon being present in the serum suggesting that it also exists as a secretory protein.

In contrast, Applicants' 3C4 Ag is a single band of 42-43.5Kd. *See* page 57, first two lines of Applicants' specification, "The fact that reduction does not change the migration pattern of 3C4-Ag indicates that the antigen does not contain subunits." 3C4 Ag is not an asialoglycoprotein. The 3C4 Ag is not found in the nucleus or nuclear extract of pancreatic cancer cells. As discussed thoroughly *supra*, 3C4-Ag is expressed preferentially on the plasma membrane of pancreatic cancer cells but little or not at all on colon cancer cells or cell lines, gastric cancer cells or any other epithelial cancer cells or cell lines and not at all found on normal cell of the exocrine pancreas.

Based on the foregoing remarks and amendments, withdrawal of the rejection of claims 1 and 3 as allegedly obvious over Glassy et al. is respectfully requested.

Accordingly, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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